Poly(α-n-alkyl-L-aspartate)s: a new family of helical nylons*

F. López-Carrasquero, M. García-Alvarez and S. Muñoz-Guerra†
Departamento de Ingeniería Química, Universidad Politécnica de Cataluña, ETS de Ingenieros Industriales, Diagonal 647, 08028 Barcelona, Spain

A number of poly(α-n-alkyl-L-aspartate)s, which are nylon-3 derivatives with an alkoxycarbonyl side group attached to every repeat unit, have been prepared by non-assisted anionic polymerization of the corresponding (*S*)-4-alkoxycarbonyl-2-azetidinones. Side reactions leading to imidation were found to take place to an extent which is highly dependent on both the polarity of the polymerization solvent and the nature of the alkyl side chain. Highly stereoregular polymers without detectable imidation and molecular weights in the range 10^5 to 5×10^5 were obtained in dimethyl sulfoxide for $n=4$, 6, 8 and 12 and in CH_2Cl_2 for $n=1$, 2 and 18 (n = number of carbon atoms in the alkyl side group). A study of the thermal stability of these new polyamides showed that they melt with decomposition to largely imidated polymers when heated at temperatures above 250°C. X-Ray analysis of oriented samples revealed that members with $n=1$, 2, 4 and 8 are able to form crystal structures with chains arranged in a helical conformation similar to the α-helix typical of polypeptides. This type of conformation seems also to be adopted by all other members of the series. For $n=6$ and 12, however, the polymer chains did not crystallize but they became aligned side by side with alkyl side groups remaining in a disordered state.

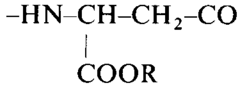
(Keywords: poly(α-n-alkyl-L-aspartate)s; anionic polymerization; helical conformation)

INTRODUCTION

Some years ago we reported on certain nylon-3 and nylon-4 derivatives which are able to adopt helical conformations similar to the characteristic α-helix of polypeptides and proteins[1-3]. The modification introduced into the constitution of these nylons involved attaching a stereoregular alkoxycarbonyl group to the backbone β-carbon or γ-carbon of every repeat unit. So far most of the studies which have been performed on this new type of nylons have dealt with poly(α-isobutyl-L-aspartate), so that a fair amount of knowledge on this polymer is now available[4]. It crystallizes in two interconvertible helical structures, hexagonal and tetragonal, made up of 13/4 and 4/1 α-type helices, respectively, generates lyotropic cholesteric liquid crystal phases and displays a remarkable piezoelectric response. The occurrence of these interesting properties is without precedent in conventional nylons and has prompted us to investigate whether such behaviour is shared by other members of the family.

An enormous amount of work has been done during the last four decades on alkyl esters of both poly(α-L-aspartic acid) and poly(α-L-glutamic acid), which are polymers closely related to the poly(α-n-alkyl-L-aspartate)s. It is well known that the constitution of the alkyl group exerts a decisive influence on the structure and properties of these homopolypeptides[5]. Aspects such as chain conformation, crystal structure, solubility and thermal properties are largely determined by the length of the alkyl side chain. Recently, Watanabe *et al.*[6] have shown that poly(α-L-glutamate)s with long n-alkyl side chains are able to form thermotropic mesophases.

In this paper we report on the synthesis, characterization and structural behaviour in the solid state of a series of poly(α-n-alkyl-L-aspartate)s (PAALAs) with linear alkyl side chains containing a number n of carbons in the alkyl group ranging from 1 to 18. These polymers are shown by the following general chemical structure:



$$\text{-HN-}\underset{\displaystyle \text{COOR}}{\underset{|}{\text{CH}}}\text{-CH}_2\text{-CO-}$$

$$R = CH_3, C_2H_5, C_4H_9, C_6H_{13}, C_8H_{17}, C_{12}H_{25}, C_{18}H_{37}$$

Early syntheses of esters of poly(β-L-aspartic acid) were carried out either by means of the *N*-carboxyanhydride method[7] or by polycondensation of active esters[8-10]. In either case low molecular weight polymers were invariably obtained. Later on, different authors[11,12] used the anionic ring-opening polymerization of β-lactams to prepare poly(α-benzyl-L-aspartate) and, more recently, poly(α-isobutyl-L-aspartate)[13,14]. This is in fact the methodology we have followed here for the synthesis of PAALAs. The corresponding (*S*)-4-alkoxycarbonyl-2-azetidinones to be used as monomers were prepared from L-aspartic acid by the method developed by Rodríguez-Galán *et al.*[12]. Particular attention has been given to the prevention of side reactions that lead to a loss in regularity

---

[*] Presented at 'The Polymer Conference', 20–22 July 1993, University of Cambridge, UK

[†] To whom correspondence should be addressed

0032-3861/94/21/4502-09

of the polymer chain. As a result, a method of synthesis of general value for the preparation of high molecular weight esters of poly(β-L-aspartic acid) in satisfactory yields has been devised.

An extensive characterization of the new PAALAs has been carried out in the present work. This includes a thermal study addressed at evaluating the stability of the polymers as a function of the side-chain size. A systematic X-ray analysis has also been performed in order to reveal the influence of the side-chain length on both the conformation and crystal structure. We present here results which show that the ability to generate conformations of the α-helix type is a property common to the whole series of PAALAs.

EXPERIMENTAL

Materials

All reagents and solvents were PA grade or higher. L-Aspartic acid ($[\alpha]_D^{25} = +24.7 \pm 0.5$, $c = 5$ in 5 N HCl) was supplied by Fluka. All solvents were exhaustively dried according to standard procedures[15].

Melting points of organic compounds were measured on a Gallenkamp apparatus and are uncorrected. Infra-red spectra were registered on a Perkin–Elmer 783 or 2000 instrument from samples in KBr discs or films prepared by casting. N.m.r. spectra were recorded on either a Varian XL-GEM-200 or a Bruker AMX-300 instrument from samples dissolved in deuterated chloroform–trifluoroacetic acid mixtures and using tetramethylsilane as internal standard. Microanalyses were performed by Servei de Microanàlisi (CSIC, Barcelona). Thermal analyses were carried out on a Mettler TA-4000 at heating rates of 10°C min^{-1} and under a nitrogen atmosphere. X-Ray diffraction diagrams were obtained in a Statton camera using nickel-filtered copper radiation with $\lambda = 0.1542$ nm. Calibration was performed with molybdenum sulfide ($d_{002} = 0.6147$ nm).

Monomer synthesis

(S)-4-Benzyloxycarbonyl-2-azetidinone **III** was prepared according to the method of Salzmann[16]. The general procedure used for transesterification of this compound was as follows. A stirred solution of **III** (0.1 mol) in the corresponding alcohol at a molar ratio between 1 and 0.25 and containing 0.03 mol of titanium tetrabutoxide was heated at a temperature in the range 80–100°C for a period of time between 2 and 4 h under a nitrogen atmosphere. The reaction mixture was then diluted with two volumes of chloroform and successively washed with 1 N HCl, 2% sodium hydrogen carbonate and water in order to remove the catalyst. This operation was avoided in the preparation of **IVa** and **IVb** since these compounds are water soluble. Evaporation of the chloroform solution afforded an oily residue from which compounds **IVa**–**IVe** were isolated by distillation under vacuum and **IVf** and **IVg** by precipitation. All monomers were finally purified to the correct elemental analysis by repeated crystallization.

Polymerization of (S)*-4-alkoxycarbonyl-2-azetidinones IV: general procedure for the synthesis of poly(α-n-alkyl-L-aspartate)s*

All polymerization reactions were run under a nitrogen atmosphere at room temperature. The method slightly differed according to the solvent used for the polymerization. In the case of dimethyl sulfoxide (DMSO) the procedure was as follows. To a stirred solution of β-lactam **IV** in DMSO was added about three volumes of a solution of sodium pyrrolidone in the same solvent by means of a syringe. The concentrations of such solutions were adjusted to give finally a monomer concentration of 18% (w/w) and a molar ratio of catalyst to monomer of 4×10^{-2}. Within a few minutes the originally colourless solution became pink and gel-like. The polymerization was left to proceed for 24 h, after which the reaction mixture was diluted with an equal volume of fresh solvent and the reaction stopped by adding six volumes of methanol. By this means the polymer precipitated as a white solid that was separated by centrifugation and repeatedly washed with methanol. Final purification was accomplished by dissolving the polymer in either chloroform or a chloroform–trifluoroacetic acid mixture and precipitating it by addition of methanol. All polymers were thoroughly dried in an oven under vacuum. When the polymerization was carried out in CH_2Cl_2, the catalyst was added as a powder in the calculated amount and the viscosity of the mixture was observed to increase gradually throughout the whole reaction time. Isolation and purification of the polymer were performed as before.

Poly(α-methyl-L-aspartate). To a vigorously stirred solution of compound **IVa** (1.2 g, 9.3 mmol) in CH_2Cl_2 (5 ml) was added solid sodium pyrrolidone (0.004 g, 0.04 mmol). After isolation and purification according to the general procedure, the title polymer was obtained in 82% yield. ^{1}H n.m.r. (ppm) 8.05 (d, 1H, $\mathrm{N\underline{H}}$), 4.95 (m, 1H, β-$\mathrm{C\underline{H}}$), 3.80 (s, 3H, $\mathrm{C\underline{H}_3}$) and 3.15 (m, 2H, α-$\mathrm{C\underline{H}_2}$). ^{13}C n.m.r. (ppm) 173.15, 172.80, 54.13, 49.97 and 36.80. Analysis calculated for $(C_5H_7NO_3)_n$: C, 46.51; H, 5.47; N, 10.85. Found: C, 45.64, H, 5.45; N, 10.76.

Poly(α-ethyl-L-aspartate). In the same manner as given above, the title polymer was obtained from compound **IVb** in 68% yield. ^{1}H n.m.r. (ppm) 8.05 (d, 1H, $\mathrm{N\underline{H}}$), 4.95 (m, 1H, β-$\mathrm{C\underline{H}}$), 4.29 (q, 2H, $\mathrm{COOC\underline{H}_2}$), 3.15 (m, 2H, α-$\mathrm{C\underline{H}_2}$) and 1.28 (t, 3H, $\mathrm{C\underline{H}_3}$). ^{13}C n.m.r. (ppm) 172.67, 172.49, 64.33, 49.93, 49.93, 36.70 and 13.07. Analysis calculated for $(C_6H_9NO_3)_n$: C, 50.35; H, 6.34; N, 9.47. Found: C, 49.05, H, 6.10; N, 9.64.

Poly(α-n-butyl-L-aspartate). To a stirred solution of **IVc** (1 g, 5.84 mmol) in DMSO (1.4 ml) was added 3.6 ml of a solution of sodium pyrrolidone in the same solvent (7.6 mg ml^{-1}). After purification the title polymer was obtained in 56% yield. ^{1}H n.m.r. (ppm) 8.10 (d, 1H, $\mathrm{N\underline{H}}$), 4.90 (m, 1H, β-$\mathrm{C\underline{H}}$), 4.22 (t, 2H, $\mathrm{COOC\underline{H}_2}$), 3.20 (m, 2H, α-$\mathrm{C\underline{H}_2}$), 1.62 (m, 2H, $\mathrm{COOCH_2C\underline{H}_2}$), 1.34 (m, 2H, $\mathrm{C\underline{H}_2CH_3}$) and 0.90 (t, 3H, $\mathrm{C\underline{H}_3}$). ^{13}C n.m.r. (ppm) 172.06, 171.48, 67.29, 49.51, 36.49, 30.00, 18.67 and 13.18. Analysis calculated for $(C_8H_{13}NO_3)_n$: C, 56.13; H, 7.65; N, 8.18. Found: C, 56.03, H, 7.47; N, 8.29.

Poly(α-n-hexyl-L-aspartate). In substantially the same manner as given above, the title polymer was obtained in 52% yield from 1.0 g of compound **IVd**. ^{1}H n.m.r. (ppm) 8.00 (d, 1H, $\mathrm{N\underline{H}}$), 4.85 (m, 1H, β-$\mathrm{C\underline{H}}$), 4.17 (m, 2H, $\mathrm{COOC\underline{H}_2}$), 3.10 (m, 2H, α-$\mathrm{C\underline{H}_2}$), 1.63 (m, 2H, $\mathrm{COOCH_2C\underline{H}_2}$), 1.30 (br s, 6H, $\mathrm{COOCH_2CH_2(C\underline{H}_2)_3}$)

and 0.97 (t, 3H, $C\underline{H}_3$). ^{13}C n.m.r. (ppm) 172.09, 171.50, 67.64, 49.56, 36.47, 31.14, 27.97, 25.08, 22.31 and 13.64. Analysis calculated for $(C_{10}H_{17}NO_3)_n$: C, 60.28; H, 8.36; N, 7.03. Found: C, 59.43, H, 8.36; N, 7.40.

Poly(α-n-octyl-L-aspartate). As above, the title polymer was obtained in 70% yield from 1.0 g of compound **IVd**. ^1H n.m.r. (ppm) 8.00 (d, 1H, N$\underline{H}$), 4.89 (m, 1H, β-C$\underline{H}$), 4.18 (m, 2H, $COOC\underline{H}_2$), 3.10 (m, 2H, α-$C\underline{H}_2$), 1.63 (m, 2H, $COOCH_2C\underline{H}_2$), 1.27 (br s, 10H, $COOCH_2CH_2(C\underline{H}_2)_5$) and 0.90 (t, 3H, $C\underline{H}_3$). ^{13}C n.m.r. (ppm) 172.84, 172.67, 68.27, 49.74, 36.57, 31.78, 29.81, 29.10, 28.08, 25.48, 22.60 and 13.71. Analysis calculated for $(C_{12}H_{21}NO_3)_n$: C, 63.41; H, 9.25; N, 6.17. Found: C, 63.55; H, 9.40; N, 6.12.

Poly(α-n-dodecyl-L-aspartate). This polymer was prepared in 74% yield from compound **IVe** by following the general procedure. ^1H n.m.r. (ppm) 8.00 (d, 1H, N$\underline{H}$), 4.89 (m, 1H, β-C$\underline{H}$), 4.19 (m, 2H, $COOC\underline{H}_2$), 3.10 (m, 2H, α-$C\underline{H}_2$), 1.63 (m, 2H, $COOCH_2C\underline{H}_2$), 1.27 (br s, 18H, $COOCH_2CH_2(C\underline{H}_2)_9$ and 0.88 (t, 3H, $C\underline{H}_3$). ^{13}C n.m.r. (ppm) 172.46, 68.37, 49.81, 36.66, 32.07, 29.75, 29.57, 29.24, 28.17, 25.60, 22.77 and 13.87. Analysis calculated for $(C_{16}H_{29}NO_3)_n$: C, 67.81; H, 10.31; N, 4.94. Found: C, 67.61; H, 10.34; N, 4.80.

Poly(α-n-octadecyl-L-aspartate). To a solution of compound **IVg** (1.08 g, 2.94 mmol) in CH_2Cl_2 (6 ml) was added solid sodium pyrrolidone (0.012 g, 0.12 mmol) with vigorous stirring. After isolation and purification in the usual manner, the title polymer was obtained in 57% yield. ^1H n.m.r. (ppm) 8.00 (d, 1H, N$\underline{H}$), 4.84 (m, 1H, β-C$\underline{H}$), 4.13 (m, 2H, $COOC\underline{H}_2$), 3.10 (m, 2H, α-$C\underline{H}_2$), 1.59 (m, 2H, $COOCH_2C\underline{H}_2$), 1.20 (br s, 30H, $COOCH_2CH_2(C\underline{H}_2)_{15}$ and 0.90 (t, 3H, $C\underline{H}_3$). ^{13}C n.m.r. (ppm) 173.07, 171.44, 67.64, 49.68, 36.66, 32.01, 29.80, 29.75, 29.70, 29.56, 29.45, 29.23, 28.19, 25.61, 22.75 and 14.11. Analysis calculated for $(C_{22}H_{41}NO_3)_n$: C, 71.89; H, 11.24; N, 3.81. Found: C, 70.77; H, 11.24; N, 3.71.

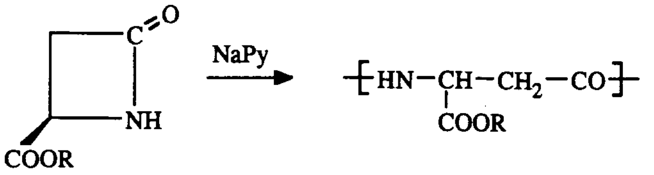
RESULTS

Monomer synthesis

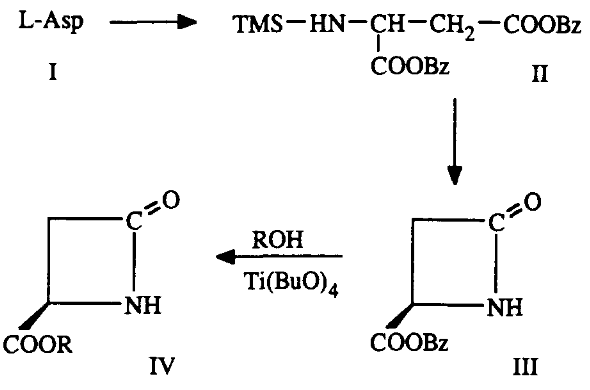
The synthetic route we have followed for the preparation of the β-lactam monomers is shown in *Scheme 1*. It is based on the Grignard-mediated cyclization of the *N*-trimethylsilylated dibenzyl L-aspartate **II** giving (*S*)-4-benzyloxycarbonyl-2-azetidinone **III**[16]. Compound **II** is readily obtained from L-aspartic acid **I** in three steps. Compound **III** is then subjected to transesterification[12] with linear alcohols in the presence of titanium tetrabutoxide to give the analogous (*S*)-4-alkoxycarbonyl-2-azetidinones **IV**. By using this procedure, a number of new optically active, monosubstituted β-lactams were readily prepared, and the yields and physical constants are collected in *Table 1*. All these compounds were crystalline and susceptible to purification by repeated crystallization. A plot of melting point against the number of carbon atoms contained in the alkyl group shows how the melting points slide down into a minimum for intermediate values of the chain length (*Figure 1*). As will be discussed below, a similar trend is observed for the crystallinity of the corresponding polymers. These β-lactams were obtained in high optical purity, assessed by checking the optical rotation of the L-aspartic acid generated in their hydrolysis. As expected, a steady decrease in specific optical rotation with increasing size of the side chain through dilution effects is observed along the whole series (*Figure 1*). A detailed account of the synthesis and characterization of this family of (*S*)-4-alkoxycarbonyl-2-azetidinones, including members with linear, branched and cyclic alkyl groups, will be reported elsewhere.

Polymer synthesis and characterization

β-Lactams **IVa**–**IVg** were anionically polymerized in solution at room temperature to give a series of stereoregular nylons-3 containing an alkoxycarbonyl group attached to every β-carbon atom of the polymer backbone:



Sodium pyrrolidone was used as the anionic catalyst and no *N*-acyllactam of the type commonly used as chain initiator in the anionic polymerization of lactams was added. High purity of monomers and solvents and



TMS =Trimethylsilyl; Bz = $CH_2C_6H_5$

Scheme 1

Table 1 (*S*)-4-Alkoxycarbonyl-2-azetidinones **IV**: yields, melting points and specific optical rotations

Azetidinone	**IVa**	**IVb**	**IVc**	**IVd**	**IVe**	**IVf**	**IVg**
R	CH_3	C_2H_5	C_4H_9	C_6H_{13}	C_8H_{17}	$C_{12}H_{25}$	$C_{18}H_{37}$
Yield (%)	64	71	69	47	58	53	51
Melting point (°C)	45–46	[a]	43–44	15–16	42–43	66–67	89–90
$[\alpha]_D^{25}$ (°)	−41.4	−39.7	−36.3	−33.6	−29.0	−22.4	−17.4

[a] Highly hygroscopic compound for which measurement of the melting point was not feasible

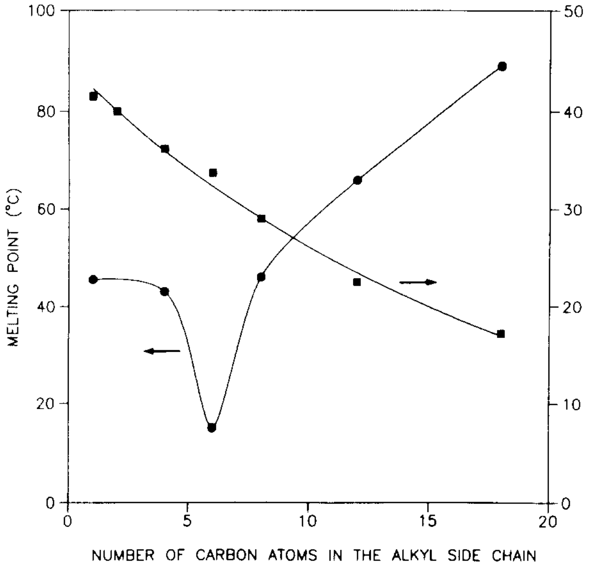


Figure 1 Melting points (●) and specific optical rotations $[\alpha]_D^{25}$ (■) ($c = 1\,g\,dl^{-1}$ in Cl_3CH) of (*S*)-4-alkoxycarbonyl-2-azetidinones as a function of the number of carbon atoms in the alkyl side chain

the total exclusion of water are requirements for a reproducible polymerization. According to Graf *et al.*[17], dimethyl sulfoxide (DMSO) is the solvent generally used in these polymerizations because it readily dissolves the catalyst, allowing a homogeneous reaction. In the polymerization of **IVa** and **IVb**, however, DMSO had to be replaced by dichloromethane (DCM) in order to suppress the formation of undesirable imide structures. DCM was also used in the polymerization of **IVg** since this compound is not completely soluble in DMSO. In DMSO the polymerization started up immediately and proceeded speedily, so that the reaction mixture became gel-like in a few minutes. In DCM the reaction rate was much slower and the viscosity of the medium increased continuously with reaction time. In either case the forming polymer remained swollen in the reaction mixture and was separated out by precipitation with methanol. By these procedures polymers with intrinsic viscosities in the range 1.2–2.9 $dl\,g^{-1}$ were obtained in yields over 50%. A summary of the polymerization data concerning all the poly(α-n-alkyl-L-aspartate)s prepared in this work is given in *Table 2*.

Elemental analyses and infra-red, ^1H n.m.r. and ^{13}C n.m.r. spectroscopic data are in full agreement with the compositions expected for these polyamides. Deviations higher than 1% in the carbon analyses were found, however, for the methyl and ethyl derivatives. This may be accounted for by assuming that these polymers contain about 1% (w/w) water, which is quite reasonable given the high hygroscopicity exhibited by their corresponding monomers. The infra-red spectra show the characteristic absorptions of polyamides (amide A 3275 cm^{-1}; amide B, 3080 cm^{-1}; amide I, 1650 cm^{-1}; amide II, 1540 cm^{-1}; amide V, 670 cm^{-1}) in addition to a strong peak at 1740 cm^{-1} arising from the C=O of the pendent carboxylate group. On the other hand, the ^1H n.m.r. spectra display signals common to the whole series at 8.1, 4.9 and 3.1 ppm corresponding to NH, CH and CH_2 backbone protons, respectively, as well as others of variable complexity arising from the alkyl side chain. Every carbon atom in the repeat unit of each PAALA has a discrete signal in the ^{13}C n.m.r. spectrum, which allows a definitive assessment of the constitutions of the polymers. In particular, the two carbonyl groups are revealed by the splitting of the downfield signal appearing at about 172 ppm and the two backbone carbons, α-CH_2 and β-CH, by singlets at 37 and 49 ppm, respectively. A full account of the n.m.r. data recorded for every polymer is given in the Experimental section. The infra-red, ^1H n.m.r. and ^{13}C n.m.r. spectra of poly(α-n-octyl-L-aspartate) are depicted in *Figure 2*.

Solvent effects

It is known that undesirable side reactions leading to imide formation may take place in the polymerization of β-lactams carrying a carboxylate group at the 4-position. The polarity of the solvent used in the polymerization has been reported to be of major importance in determining the extent to which such side reactions occur[12]. Thus (*S*)-4-benzyloxycarbonyl-2-azetidinone polymerized to polysuccinimide in dimethyl sulfoxide, whereas poly(α-benzyl-L-aspartate) practically free of imide structures was obtained when dichloromethane was the solvent of choice. Nevertheless, the constitution of the side group is known as the second factor which must be taken into account[14]. In the present work, polymerizations of β-lactams **IVc**–**IVf** were carried out in DMSO to afford polyamides with no detectable amounts of imide units. Conversely, a high degree of imidation was found in polymers prepared from β-lactams **IVa** and **IVb** under similar reaction conditions, accompanied by a drastic reduction in both the yield and molecular weight of the resulting products. It was further observed that a noticeable decrease in the imide content could be attained by shortening the polymerization time to a few minutes without reducing significantly the polymerization yield. In *Figure 3* infra-red spectra of the polymers obtained in the polymerization of (*S*)-4-methoxycarbonyl-2-azetidinone in three different experiments performed under different conditions are compared with the infra-red spectrum of pure polysuccinimide. The intense absorption at 1716 cm^{-1} with a shoulder at 1798 cm^{-1} revealed the presence of imide units in polymers prepared in DMSO and evidenced that pure poly(α-methyl-L-aspartate) could only be obtained if dichloromethane was the solvent used in the polymerization. It is feasible to make an approximate quantitative evaluation of the degree of imidation in

Table 2 Polymerization data for poly(α-n-alkyl-L-aspartate)s[a]

R	Solvent	Yield (%)	$[\eta]^b$ ($dl\,g^{-1}$) A	$[\eta]^b$ ($dl\,g^{-1}$) B	$10^{-5}M_v{}^c$ A	$10^{-5}M_v{}^c$ B
CH_3	DCM	82	2.88		5.8	2.5
C_2H_5	DCM	68	2.66	–	5.3	2.3
C_4H_9	DMSO	56	1.95	–	3.7	1.5
C_6H_{13}	DMSO	52	1.21	–	2.1	0.8
C_8H_{17}	DMSO	70	2.24	–	4.4	1.8
$C_{12}H_{25}$	DMSO	74	2.16	2.70	4.2	1.7
$C_{18}H_{37}$	DCM	58	–	1.61	–	–

[a] Polymerization conditions: lactam concentration $[M]_0$ 18% w/w; catalyst concentration 4×10^{-2} mol NaPy per mole lactam; reaction time 24 h at room temperature

[b] Intrinsic viscosity measured at 25°C in (A) dichloroacetic acid (DCA) or (B) a mixture of chloroform and dichloroacetic acid (2:1)

[c] Molecular weight estimated on the basis of viscosimetric data obtained in DCA by using the parameters of the equation reported for poly(γ-benzyl-L-glutamate)[18] (A) and poly(γ-methyl-L-glutamate)[19] (B)

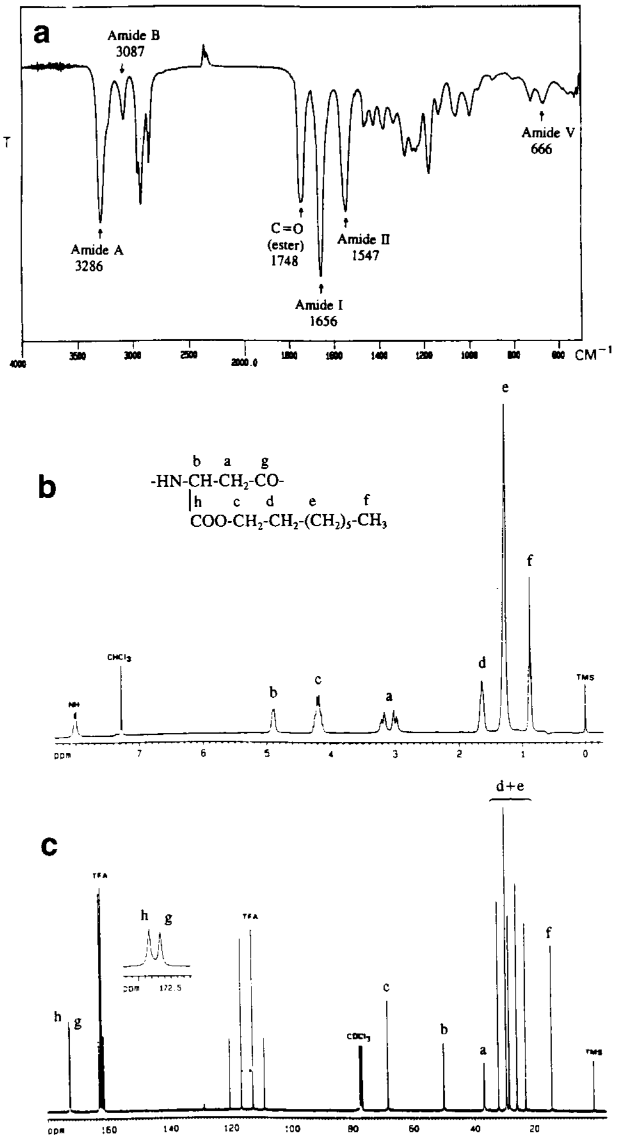


Figure 2 Spectra of poly(α-n-octyl-L-aspartate): (a) infra-red spectrum of a film prepared by casting from chloroform; (b) ^1H n.m.r. (200 MHz) spectrum in Cl_3CD–trifluoroacetic acid; (c) ^{13}C n.m.r. spectrum (75.5 MHz) in the same solvent

poly(α-n-alkyl-L-aspartate)s from the nitrogen content found in the combustion analysis. By this means, imide contents between 30 and 70% were calculated for poly(α-methyl-L-aspartate) obtained in DMSO, whereas the imide content was less than 1% for the polymer prepared in dichloromethane. Similar values were deduced from the ^1H n.m.r. spectra by comparing the areas of the α-CH_2 signals corresponding to β-aspartamide and aspartimide units. A summary of the solvent effects observed in the polymerization of β-lactams **IVa** and **IVb**, together with those reported earlier for poly(α-benzyl-L-aspartate), is given in *Table 3*.

Thermal stability

The thermal behaviour of the PAALAs largely varies from one member to another depending on the length of the alkyl side chain. In some cases the differential scanning calorimetry (d.s.c.) scan appeared rather complex owing to the occurrence of multiple transitions involving structural changes either in the solid state or in the mesophase. Such complexity deserves a specific investigation and this is currently under way. In accordance with the context of the present work we will restrict this study to the investigation of the thermal stability of PAALAs.

The d.s.c. traces from all these polymers at temperatures above 200°C exhibited a prominent endotherm in the range 240–350°C which could be initially attributed to the melting of the polymer. On the other hand, the thermogravimetric analysis (t.g.a.) showed that decomposition began at temperatures close to 240°C, accompanied by a loss of the initial sample weight amounting to 70–90% above 380°C. The decomposition process was found to take place in two stages: the first at a temperature steadily increasing from 260°C for

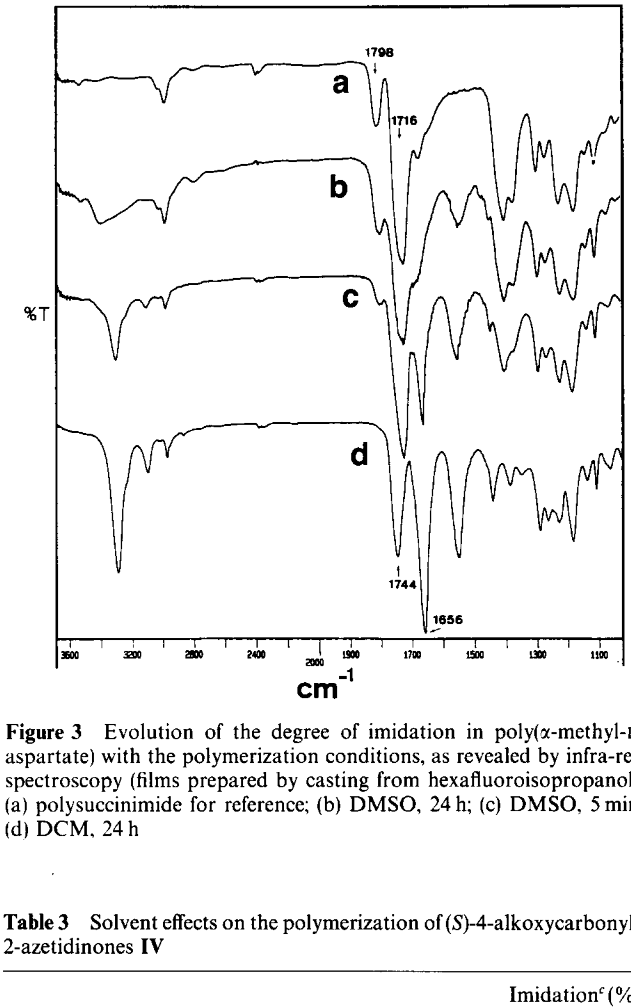


Figure 3 Evolution of the degree of imidation in poly(α-methyl-L-aspartate) with the polymerization conditions, as revealed by infra-red spectroscopy (films prepared by casting from hexafluoroisopropanol): (a) polysuccinimide for reference; (b) DMSO, 24 h; (c) DMSO, 5 min; (d) DCM, 24 h

Table 3 Solvent effects on the polymerization of (*S*)-4-alkoxycarbonyl-2-azetidinones **IV**

R	Solvent	Yield (%)	[η][a] (dl g⁻¹)	N content[b] (%)	Imidation[c] (%) A	Imidation[c] (%) B
CH_3	DCM	81	2.9	10.76	<1	n.d.
CH_3	DMSO	24	0.16	12.70	60	70
CH_3	DMSO	23	0.71	11.65	30	38
C_2H_5	DCM	68	2.7	9.79	<1	n.d.
C_2H_5	DMSO	33	0.10	12.22	70	90
C_6H_5[d]	DCM	83	3.50	6.91	<5	–
C_6H_5[d]	DMSO	46	0.10	11.28	90	–

[a] Intrinsic viscosity measured in dichloroacetic acid at 25°C
[b] Nitrogen content determined by combustion analysis. Calculated values for each polymer are given in the Experimental section and elsewhere[12]. For polysuccinimide the calculated nitrogen content is 14.43%
[c] Percentage of aspartimide units calculated on the basis of nitrogen analysis (A) and ^1H n.m.r. signal area (B) (n.d. = not detectable)
[d] Data taken from the literature[12]

Table 4 D.s.c. and t.g.a. data for poly(α-n-alkyl-L-aspartate)s

R	T_m/T_d[a] (°C)	T_{d1}[b] (°C)	T_{d2}[b] (°C)	Weight loss (% w/w): Observed[c] for First stage	Observed[c] for Whole process	Calculated for first stage[d]
CH_3	287	261	370	29	71	24.8
C_2H_5	287	261 (312)	368	43	77	32.0
C_4H_9	282	286	377	42	78	42.2
C_6H_{13}	307	291	384	52	81	52.3
C_8H_{17}	341	326	380	57	86	57.3
$C_{12}H_{25}$	348	333	380 (s)	–	89	64.7
$C_{18}H_{37}$	330	324	380 (s)	–	92	72.0

[a] Determined by d.s.c.
[b] Determined by t.g.a.; three peaks observed for poly(α-ethyl-L-aspartate) (s = shoulder)
[c] Determined by t.g.a.
[d] Calculated as explained in the text

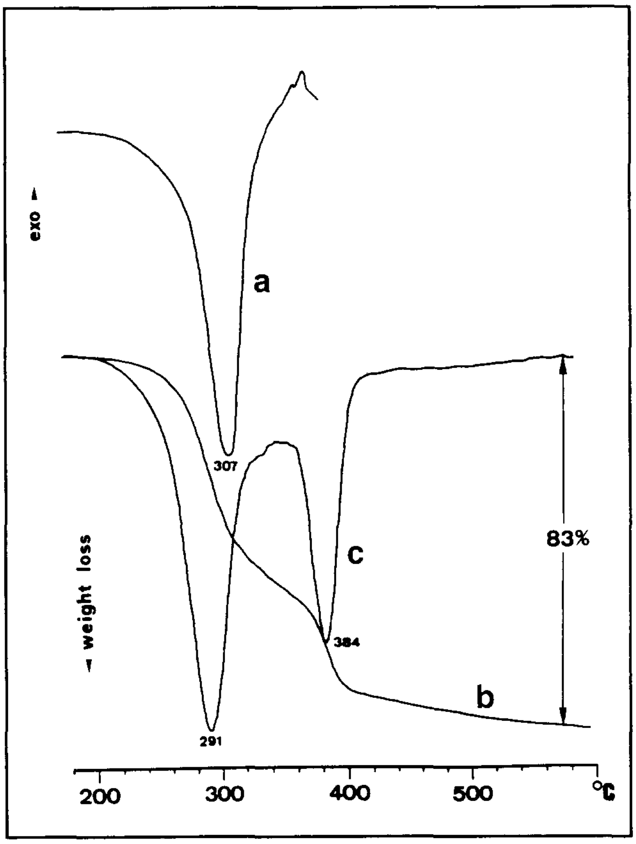


Figure 4 (a) D.s.c. and (b) t.g.a. traces from poly(α-n-hexyl-L-aspartate) in the temperature range 200–400°C. (c) Derivatized plot of (b) illustrating vividly the two decomposition stages

poly(α-methyl-L-aspartate) to about 330°C for the stearyl derivative, and the second occurring at a rather fixed temperature in the proximity of 380°C. Owing to the displacement of the first peak towards higher temperatures, the two decomposition steps are not well resolved for the higher members of the series. Both d.s.c. and t.g.a. diagrams recorded for poly(α-n-hexyl-L-aspartate) are reproduced in *Figure 4* and data obtained by these techniques for the whole series of PAALAs are gathered in *Table 4*.

Infra-red spectra recorded for PAALAs which had been subjected to heating at the temperature of the first decomposition step revealed that an extensive imidation process had taken place. On the other hand, an acceptable concordance is in general obtained between experimental and calculated weight loss values if one assumes that 1 mol of alcohol is released by every repeat unit of the polymer. Therefore it may be concluded that not only melting but also the nearly complete imidation of the polymer should contribute to the endothermic peak observed between 240 and 350°C by d.s.c. The heat flow involved in such a peak must also account for the vaporization enthalpy of the alcohol liberated in the decomposition.

Structural study

In order to investigate the structure in the solid state, oriented samples of PAALAs were examined by X-rays. Samples were prepared by stretching films cast from solutions of PAALAs in chloroform or halogenated alcohols (trifluoroethanol, 2-chloroethanol and hexafluoroisopropanol). Representative diffraction patterns are shown in *Figure 5* for $n = 4$, 8 and 12. Features of the X-ray diagrams common to the whole series are the very strong reflection appearing on the equator, which is related to the lateral packing of the polymer chains, and the prominent and broad layer line at a spacing of 0.45–0.50 nm associated with the repetition of the structure along the chain axis. It was found, however, that the level of crystallinity was highly dependent on the nature of the side chain. Diagrams containing well-resolved off-meridional reflections indicative of three-dimensional order were obtained for PAALAs with $n \leqslant 4$. A typical X-ray photograph for this class of PAALAs is shown for poly(α-n-butyl-L-aspartate) in *Figure 5a*. The pattern is fully consistent with a hexagonal structure made of 13/4 helices with $a_0 = 1.35$ nm and $c_0 = 1.99$ nm, which incidentally coincide with the values reported for the hexagonal form of poly(α-isobutyl-L-aspartate)[1]. Similar structures were deduced for the methyl and ethyl derivatives from an analysis of their respective X-ray diagrams.

Diagrams from oriented films of PAALAs with $n = 6$ and 12 (*Figure 5b*) provided no information concerning the axial arrangement of the helices along the stretching direction because of the lack of *hkl* reflections. We interpret these diagrams as arising from an oriented disordered structure in which α-helical molecules are aligned with regard to the chain direction but they are subject to random axial displacements or rotations. Although similar diagrams were initially recorded for poly(α-n-octyl-L-aspartate), a diffraction pattern with the

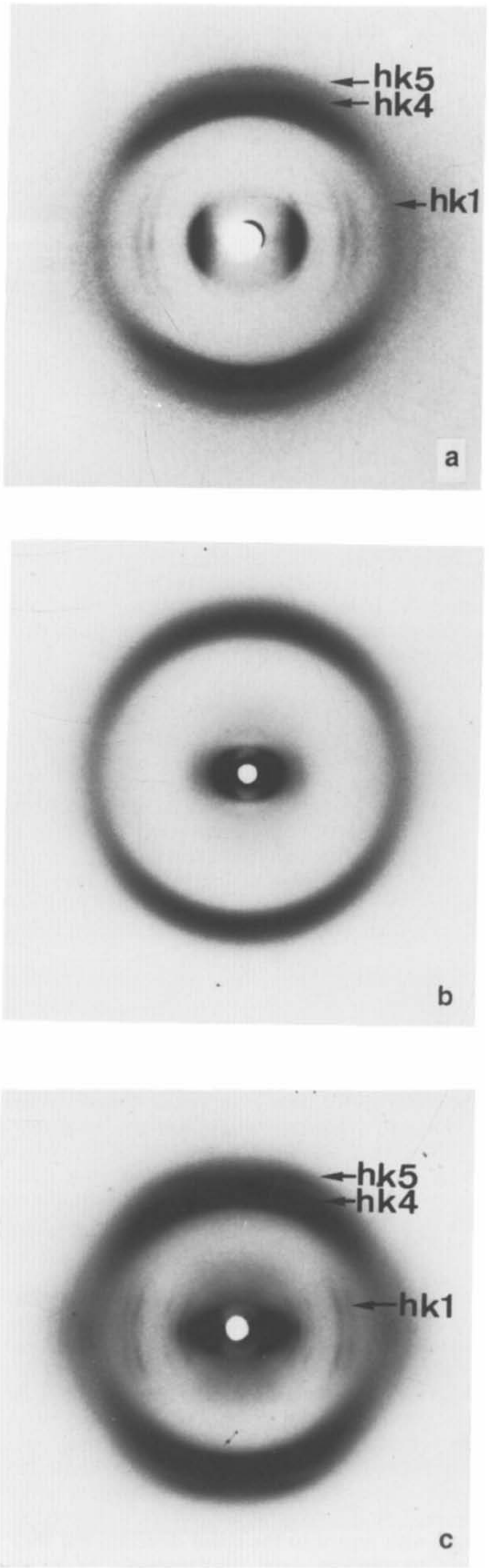


Figure 5 X-Ray photographs of (a) poly(α-n-butyl-L-aspartate), (b) poly(α-n-dodecyl-L-aspartate) and (c) poly(α-n-octyl-L-aspartate)

characteristics of those given by the lower members of the series (*Figure 5c*) was obtained when the polymer was subjected to annealing at a temperature of 108°C. In this case, however, the equatorial spacings required indexing on the basis of a rhombic or monoclinic lattice from a slightly distorted hexagonal lattice.

A different type of diagram was recorded from poly(α-n-octadecyl-L-aspartate) owing to crystallization of the long side chains. In this case the analysis of the pattern was complicated by the presence of reflections from both the n-alkane-type crystal phase and the structure made up of main chains. Nevertheless, spacings appearing in the low angle region as well as those contained in layer lines were compatible with the occurrence of chains in an α-helical conformation arranged in a layered structure of the type reported by Watanabe *et al.* for poly(γ-stearyl-L-glutamate)[6].

A list of the long spacings measured for the PAALAs, together with the observed and calculated densities for those cases in which the crystal structure could be derived, is given in *Table 5*. The plots of these data against the number of carbon atoms in the alkyl side chain (*Figure 6*) show how they steadily change with the length of the side chain. The exceptionally low density for $n = 12$ could be caused by a lack of crystallinity in the sample.

DISCUSSION

The synthesis of chiral polyamides of AB type other than polypeptides is by no means straightforward. Difficulties concerning the availability of monomers and the occurrence of unexpected side reactions during polymerization are of major importance[20]. Most of the many alkyl esters of poly(α-glutamic acid) and poly(α-aspartic acid) which have been described in the literature[5] were prepared by transesterification of the side chain of the polymer, usually in the easily available poly(γ-methyl-L-glutamate) and poly(β-methyl-L-aspartate), respectively. By this method random copolymers containing a mixture of methyl and other alkyl side chains are readily obtained. Our work concentrates on the synthesis of highly stereoregular homopolymers through the polymerization of well-characterized monomers.

Undoubtedly the anionic ring-opening polymerization of β-lactams as described by Graf *et al.*[17] appears to be the most efficient method of preparing high molecular weight nylon-3 derivatives in satisfactory yields. In this method, β-lactam monomers are prepared by 1,2-dipolar electrophilic addition of chlorosulfonyl isocyanate to alkenes. This reaction is not expected to be applicable to the preparation of alkoxycarbonyl derivatives because of the low nucleophilicity of the acrylate derivatives which would be used as substrates for the cycloaddition. Moreover, racemic mixtures will be furnished by this method if a chiral centre is generated in the cycloaddition reaction. The method we have applied for the preparation of the monomers combines cyclization of the benzyl aspartate diester[16] with the titanium-mediated transesterification technique developed by Seebach *et al.*[21]. Our attempts to obtain directly the 4-alkoxycarbonyl-β-lactams by cyclization of the analogous *N*-silylated L-aspartate diesters in the same manner as 4-benzyloxycarbonyl-2-azetidinone was prepared by Salzmann *et al.*[16] were unfruitful. Fortunately, transesterification of this compound has been found to be a valuable route to

Table 5 Structural data for poly(α-n-alkyl-L-aspartate)s

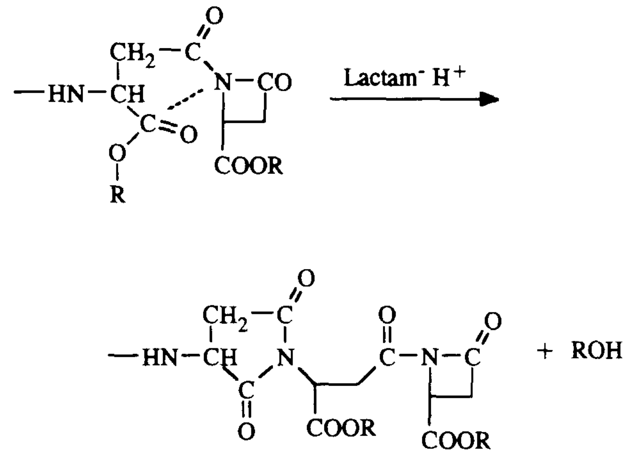
R	CH_3	C_2H_5	C_4H_9	C_6H_{13}	C_8H_{17}	$C_{12}H_{25}$	$C_{18}H_{37}$
L_0[a] (nm)	1.04	1.07	1.17	1.6	1.9, 1.2, 1.0	2.5	3.1
ρ (g ml^{-1})							
Observed[b]	1.36	1.26	1.17	1.07	1.06	0.99	1.03
Calculated[c]	1.36	1.26	1.18	–	1.06	–	–
Crystal form	Hexagonal	Hexagonal	Hexagonal	–	Hexagonal (distorted)[d]	–	–

[a] Long spacing appearing on the equator of the X-ray diagram
[b] Measured by the flotation method in water–KBr solution mixtures
[c] Calculated for the respective crystal lattice; for n-octyl, calculated by assuming an orthogonal lattice of 1.9 × 1.2 nm
[d] Crystallized by annealing at 108°C

obtaining our monomers in high purity and satisfactory yields.

In contrast to the usual procedures followed in the polymerization of higher lactams, the polymerizations of 4-alkoxycarbonyl-β-lactams were conducted without a chain initiator. It is known that the electron-withdrawing carboxylate group on the ring enhances the reactivity of these β-lactams towards the anionic ring-opening polymerization. Since the reaction may start without the participation of *N*-acyl derivatives a polymerization mechanism initiated by the monomer itself as the sodium salt could be reasonably invoked. This implies that the function of sodium pyrrolidone is to generate the azetidinone anion by acid–base exchange. Such a mechanism would be able to explain the decrease in both molecular weight and polymerization yield which is observed when high concentrations of catalyst are used[14].

Imide formation in the polymerization of 4-alkoxycarbonyl-β-lactams is assumed to take place according to the following mechanism[12]:



We have observed that this reaction proceeds to a considerable extent for the ethyl and methyl derivatives if a polar solvent such as DMSO is used. No plausible explanation can be given so far to account for the relationship existing between the constitution of the side group and the tendency towards imidation. On the other hand, the fact that such a reaction could be significantly suppressed by reducing the time for which the polymer was in contact with the reaction medium suggests that the above mechanism may not be the only one contributing to the imidation process.

The thermal studies on the stability of PAALAs have revealed that the melting of the polymer is accompanied by a large loss in weight. Furthermore, they have shown that imidation is again the reaction involved in the thermal decomposition of these polymers. It is obvious that in this case imide formation must proceed by the electrophilic attack of the side carbonyl group at the NH placed on the next repeat unit without requiring the participation of the end β-lactam cycle as proposed elsewhere for explaining imidation in growing chains[12]. Therefore we consider such a mechanism to be the main one, if not the only one, operating in the imidation of the methyl and ethyl derivatives obtained in polymerizations carried out in DMSO.

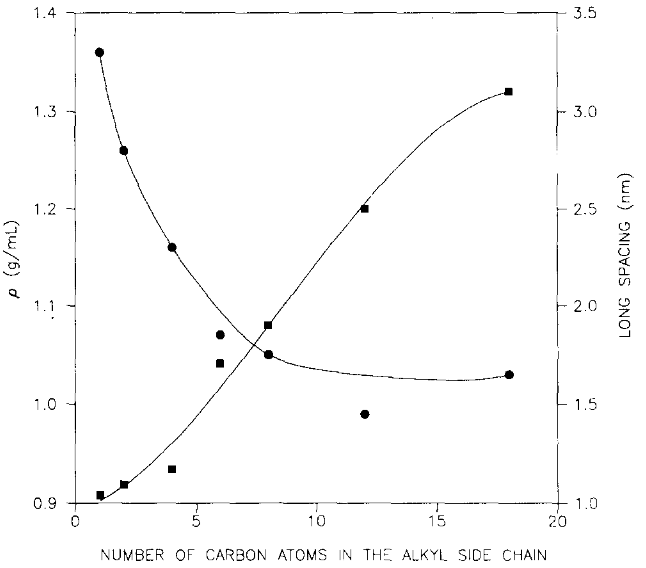


Figure 6 Long spacings (■) and observed densities (●) of PAALAs as a function of the number of carbon atoms in the alkyl side chain. Deviations observed in density for $n=6$ and 12 correlate well with the lack of three-dimensional order exhibited by these polymers. For $n=8$ the density was measured on an annealed sample (see the text)

No data are provided that give any indication of the decomposition mechanism at temperatures above 350°C. Nevertheless, it is reasonable to assume that radical reactions involving scission of the polyimide backbone should be dominant therein. This is in fact the mechanism reported for the decomposition of poly(γ-methyl-L-glutamate) at such temperatures[22].

PAALAs with $n \leqslant 4$ show structural behaviour very similar to that of poly(α-isobutyl-L-aspartate), for which the existence of conformations of the α-helix type has been demonstrated. In fact the X-ray diagram of the hexagonal crystal form of this polymer and that obtained from poly(α-n-butyl-L-aspartate) are practically indistinguishable. Furthermore, traces of a second crystal form, probably tetragonal, have been occasionally encountered in this study. X-Ray patterns from the methyl and ethyl derivatives also display the features of a helical hexagonal structure with parameters in agreement with those expected from the respective side-chain sizes.

PAALAs containing n-alkyl side chains of intermediate lengths ($4<n\leqslant 12$) appear reluctant to crystallize. This is the same situation as found for the analogous esters of poly(α-L-aspartic acid) and poly(α-L-glutamic acid)[23,24], which is currently interpreted as being a result of the high mobility of the side chain in the range of temperatures under observation. However, the long equatorial spacings measured for these polymers, as well as the intense layer line at 0.45–0.5 nm characteristic in the X-ray patterns, strongly suggest that they are arranged in a helical conformation. The structure is viewed as being composed of rigid α-helical backbones with attached side chains remaining in a liquid disordered state. Poly(α-n-octyl-L-aspartate) was unique in crystallizing by annealing to yield a three-dimensional structure similar to that observed for the lower members. The fact that the hexyl derivative could not be crystallized by this treatment is an unexpected result for which no plausible explanation can be given at this time.

The highest member of the PAALAs studied in the present work, poly(α-stearyl-L-aspartate), shows close similarities to its homologous poly(α-L-glutamate)[6]. In this polymer, backbone chains and alkyl side groups crystallize separately in a two-phase structure with molecules presumably adopting an α-type helical conformation. By analogy, the structure will consist of an array of layers made up of rigid α-helices separated by a crystalline paraffinic interphase with a repeat distance of 3.1 nm.

ACKNOWLEDGEMENTS

This research was supported by the Dirección General Científica y Técnica (grant PB90-0597). We are indebted to Professor S. Montserrat for his invaluable help in the calorimetry studies. F. López-Carrasquero thanks the Venezuelan institutions Universidad de los Andes and Fundayacucho for financial assistance.

REFERENCES

1 Fernández-Santín, J. M., Aymamí, J., Rodríguez-Galán, A., Muñoz-Guerra, S. and Subirana, J. A. *Nature* 1984, **311**, 53

2 Fernández-Santín, J. M., Muñoz-Guerra, S., Rodríguez-Galán, A., Aymamí, J., Lloveras, J. and Subirana, J. A. *Macromolecules* 1987, **20**, 62

3 Puiggalí, J., Muñoz-Guerra, S., Rodríguez-Galán, A. and Subirana, J. A. *Makromol. Chem., Macromol. Symp.* 1988, **20**/**21**, 167

4 Muñoz-Guerra, S. *Makromol. Chem., Macromol. Symp.* 1991, **48**/**49**, 71

5 Block, H. 'Poly(γ-Benzyl-L-Glutamate) and Other Glutamic Acid Containing Polymers', Gordon and Breach, New York, 1983

6 Watanabe, J., Ono, H., Uematsu, I. and Abe, A. *Macromolecules* 1985, **18**, 2141

7 Kovacs, J., Ballina, R. and Rodin, R. *Chem. Ind.* 1963, 1955

8 Kovacs, J., Ballina, R., Rodin, R., Balasubramanian, D. and Applequist, J. *J. Am. Chem. Soc.* 1965, **87**, 119

9 Hardy, P. M., Haylock, J. and Rydon, H. *J. Chem. Soc., Perkin Trans. 1* 1972, 605

10 Yuki, H., Okamoto, Y., Taketani, Y. and Tsubota, *J. Polym. Sci., Polym. Chem. Edn* 1978, **16**, 2237

11 Lenz, R. and Guerin, Ph. *Polym. Sci. Technol.* 1983, **23**, 219

12 Rodríguez-Galán, A., Muñoz-Guerra, S., Subirana, J. A., Chuong, B. and Sekiguchi, H. *Makromol. Chem., Macromol. Symp.* 1986, **6**, 277

13 Vives, J., Rodríguez-Galán, A. and Muñoz-Guerra, S. *Makromol. Chem. Rapid Commun.* 1989, **10**, 13

14 García-Alvarez, M., Rodríguez-Galán, A. and Muñoz-Guerra, S. *Makromol. Chem. Rapid Commun.* 1992, **13**, 173

15 Riddick, J. A. and Bunger, W. B. 'Techniques in Chemistry', 3rd Edn, Vol. II, John Wiley & Sons, New York, 1970

16 Salzmann, T. N., Ratcliffe, R. W., Christensen, B. G. and Bouffard, F. A. *J. Am. Chem. Soc.* 1980, **102**, 6163

17 Graf, R., Lohaus, G., Borner, K., Schmidt, E. and Bestian, H. *Angew. Chem.* 1962, **74**, 523

18 Doty, P., Bradbury, J. A. and Haltzer, A. M. *J. Am. Chem. Soc.* 1956, **78**, 947

19 Tanaka, S. PhD Thesis, Kyoto University, 1972

20 Sekiguchi, H. in 'Ring-Opening Polymerization' (Eds K. J. Ivin and T. Saegusa), Vol. 2, Elsevier, London, 1984, pp. 809–901

21 Seebach, D., Hungerbuhler, E., Naef, R., Schunurremberger, P., Weidmann, B. and Züger, M. *Synthesis* 1982, 138

22 Kojima, T., Kurotu, T. and Kawaguchi, T. *Macromolecules* 1986, **19**, 1281

23 Sasaki, S., Nakamura, T. and Uematsu, I. *J. Polym. Sci., Polym. Phys. Edn* 1979, **17**, 825

24 Ito, K., Kajiyama, T. and Takayanagi, M. *Polym. J.* 1977, **9**, 355